

Title: POLYNUCLEOTIDES ENCODING A BRYOPYRAN POLYKETIDE SYNTHASE (as amended)

In the Specification

At page 1, line 1, please amend the title as follows:

~~BRYOSTATINS, BRYOPYRANS AND POLYKETIDES: COMPOSITIONS AND METHODS~~
POLYNUCLEOTIDES ENCODING A BRYOPYRAN POLYKETIDE SYNTHASE

Please amend the paragraph at page 5, line 26 as follows:

b1
FIG. 14A depicts a contig map of cosmid 3A containing the beginning of the PKS cluster. Clones used for sequencing are listed at left, arrows denote the beginning and end of sequence data obtained for each clone. Bar below indicates the number of base pairs in the contig, which was generated by Sequencer, vers. 3.1. ~~FIG. 14B shows the nucleotide and amino acid sequence of the PKS cluster from clone 3A.~~

FIG. 14B shows the nucleotide (SEQ ID NO:29) and amino acid sequence (SEQ ID NO:38) of the PKS cluster from clone 3A.

Please amend the paragraph at page 5, line 32 as follows:

b2
FIG. 15A depicts a contig map of cosmid 6A downstream of 3A. ~~FIG. 15B is the contig sequences from clone 6A.~~

FIG. 15B shows contig sequences from clone 6A. Contig 2 corresponds to SEQ ID NO:30, and contig 5 corresponds to SEQ ID NO:31.

Please amend the paragraph at page 6, line 1 as follows:

b3
FIG. 16A depicts a contig map of cosmid 5A Pst A2/F4/C2 region. ~~FIG. 16B is a nucleotide sequence from clone 5A.~~

FIG. 16B shows a nucleotide sequence (SEQ ID NO:32) from clone 5A.

Please amend the paragraph at page 6, line 4 as follows:

b4
FIG. 17B is a ~~depicts nucleotide sequence sequences~~ from a portion of clone 5B. PstA4/B1 corresponds to SEQ ID NO:33, PstD4/C1 corresponds to SEQ ID NO:34, PstC1/E1 corresponds to SEQ ID NO:35, and PstE1/A3 corresponds SEQ ID NO:36.

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Please amend the paragraph at page 6, line 5 as follows:

hs
FIG. 18A depicts a contig map of T7 end of cosmid 5A, through 5B Pst A7, to the T3 end of 5B. ~~FIG. 18B is a nucleotide sequence from a portion of clone 5B.~~

FIG. 18B depicts a nucleotide sequence from a portion of clone 5B, showing bases 1-5900 of SEQ ID NO:37.

Please amend the paragraph at page 71, line 26, as follows:

be
Ways, D. K., C. A. Kukoly, J. de Vente, J. L. Hooker, W. O. Bryant, K. J. Posekany, D. J. Fletcher, P. P. Cook and P. J. Parker. (1995). MCF-7 Breast Cancer Cells Transfected with Protein Kinase C-alpha Exhibit Altered Expression of Other Protein Kinase C Isoforms and Display a More Aggressive Neoplastic Phenotype. *J. Clin. Invest.*, **95**: 1906-15.

Please amend the Abstract at page 80 as follows:

be
The present invention recognizes that marine organisms comprise nucleic acid molecules that encode polypeptides that catalyze the synthesis of bioactive compounds, such as polyketides including bryopyran rings, such as bryostatins. One aspect of the present invention is a composition including at least one nucleic acid molecule that encodes at least one polypeptide that catalyzes at least one step in the synthesis of at least one polyketide such as a bryopyran ring, ~~wherein said at least one nucleic acid molecule is derived from at least one marine organism.~~ A second aspect of the present invention is a composition including a library of nucleic acid molecules of the present invention. These nucleic acid molecules can be used in a combinatorial biosynthesis of polyketides, bryopyran rings and bryostatins. The nucleic acids may be isolated from *Bugula neritina* and/or its symbionts, including *Endobugula sertula*.